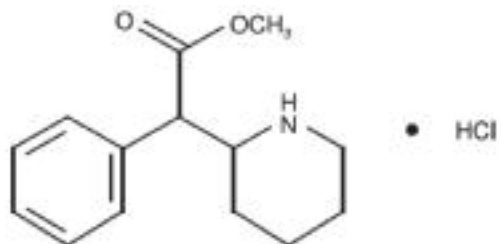


METHYLIN - methylphenidate hydrochloride tablet
METHYLIN ER - methylphenidate hydrochloride tablet
Mallinckrodt Inc.

CII
Rx Only

DESCRIPTION

Methylphenidate hydrochloride is a mild central nervous system (CNS) stimulant, available for oral administration as tablets of 5 mg, 10 mg, and 20 mg and as extended-release tablets of 10 mg and 20 mg. Methylphenidate hydrochloride is methyl α -phenyl-2-piperidineacetate hydrochloride, and its structural formula is



Methylphenidate Hydrochloride

$C_{14}H_{19}NO_2 \cdot HCl$ MW = 269.77

Methylphenidate Hydrochloride USP is a white, odorless, fine crystalline powder. Its solutions are acid to litmus. It is freely soluble in water and in methanol, soluble in alcohol, and slightly soluble in chloroform and in acetone.

Inactive Ingredients

MethylinTM tablets: lactose monohydrate, magnesium stearate, microcrystalline cellulose, and talc.

MethylinTM ER tablets: hydroxypropyl methylcellulose 2208, magnesium stearate, microcrystalline cellulose, and talc.

CLINICAL PHARMACOLOGY

Methylin is a mild central nervous system stimulant.

The mode of action in man is not completely understood, but Methylin presumably activates the brain stem arousal system and cortex to produce its stimulant effect.

There is neither specific evidence which clearly establishes the mechanism whereby Methylin produces its mental and behavioral effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system.

Methylphenidate hydrochloride in the ER tablets is more slowly but as extensively absorbed as in the regular tablets. Bioavailability of Methylin ER 20 mg Extended-Release Tablets was compared to a sustained-release reference product and an immediate-release product. The extent of absorption for the three products was similar, and the rate of absorption of the two sustained-release products was not statistically different. Relative bioavailability of the extended-release tablet compared to the immediate-release tablet, measured by the urinary excretion of methylphenidate major metabolite (α -phenyl-2-piperidine acetic acid) was 105% (49% to 168%) in children and 101% (85% to 152%) in adults. The time to peak rate in children was 4.7 hours (1.3 to 8.2 hours) for the extended-release tablets and 1.9 hours (0.3 to 4.4 hours) for the tablets. An average of 67% of extended-release tablet dose was excreted in children as compared to 86% in adults.

Based on rate of bioavailability ($AUC_{0\# \infty}$, T_{max} , and C_{max}), no significant statistical difference was found following single dose administration, in fasting and fed adults, of two Methylin ER 10 mg Extended-Release Tablets, or one methylphenidate hydrochloride sustained-release 20 mg tablet. The administration of the extended-release methylphenidate HCl tablets with food, resulted in a greater C_{max} and $AUC_{0\# \infty}$ than when administered in a fasting condition.

Pharmacokinetic and statistical analyses for a multiple dose study demonstrated that 3 times daily administration of two Methylin ER 10 mg Extended-Release Tablets met the requirements for bioequivalence to one methylphenidate hydrochloride sustained-release 20 mg tablet when administered every eight hours. Pharmacokinetic parameters (i.e., $AUC_{0\# \infty}$, T_{max} , C_{max} , C_{min} , and C_{av}) demonstrated achievement of steady state following 3 times daily administration of two Methylin ER 10 mg Extended-Release Tablets was confirmed.

In a clinical study involving adult subjects who received extended-release tablets, plasma concentrations of methylphenidate hydrochloride's major metabolite appeared to be greater in females than in males. No gender differences were observed for methylphenidate hydrochloride's plasma concentration in the same subjects.

INDICATIONS AND USAGE

ATTENTION DEFICIT DISORDERS, NARCOLEPSY

Attention Deficit Disorders (previously known as Minimal Brain Dysfunction in Children). Other terms being used to describe the behavioral syndrome below include: Hyperkinetic Child Syndrome, Minimal Brain Damage, Minimal Cerebral Dysfunction, Minor Cerebral Dysfunction.

Methylin is indicated as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate-to-severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity. The diagnosis of this syndrome should not be made with finality when these symptoms are only of comparatively recent origin. Nonlocalizing (soft) neurological signs, learning disability, and abnormal EEG may or may not be present, and a diagnosis of central nervous system dysfunction may or may not be warranted.

SPECIAL DIAGNOSTIC CONSIDERATIONS

Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

Characteristics commonly reported include: chronic history of short attention span, distractibility, emotional lability, impulsivity, and moderate-to-severe hyperactivity; minor neurological signs and abnormal EEG. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics.

Drug treatment is not indicated for all children with this syndrome. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is generally necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

CONTRAINDICATIONS

Marked anxiety, tension, and agitation are contraindications to Methylin, since the drug may aggravate these symptoms. Methylin is contraindicated also in patients known to be hypersensitive to the drug, in patients with glaucoma, and in patients with motor tics or with a family history or diagnosis of Tourette's syndrome.

Methylin is contraindicated during treatment with monoamine oxidase inhibitors, and also within a minimum of 14 days following discontinuation of a monoamine oxidase inhibitor (hypertensive crises may result).

Methylin ER is contraindicated in patients with severe hypertension, angina pectoris, cardiac arrhythmias, heart failure, recent myocardial infarction, hyperthyroidism or thyrotoxicosis (*see* **WARNINGS**).

WARNINGS

SERIOUS CARDIOVASCULAR EVENTS

SUDDEN DEATH AND PRE-EXISTING STRUCTURAL CARDIAC ABNORMALITIES OR OTHER SERIOUS HEART PROBLEMS

Children and Adolescents – Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug (*see* **CONTRAINDICATIONS**).

Adults – Sudden death, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs (*see* **CONTRAINDICATIONS**).

HYPERTENSION AND OTHER CARDIOVASCULAR CONDITIONS

Stimulant medications cause a modest increase in average blood pressure (about 2 to 4 mmHg) and average heart rate (about 3 to 6 bpm), and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia (*see* **CONTRAINDICATIONS**).

ASSESSING CARDIOVASCULAR STATUS IN PATIENTS BEING TREATED WITH STIMULANT MEDICATIONS

Children, adolescents, or adults who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

PSYCHIATRIC ADVERSE EVENTS

Pre-Existing Psychosis – Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Bipolar Illness – Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

Emergence of New Psychotic or Manic Symptoms – Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred in about 0.1% (4 patients with events out of 3,482 exposed to methylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.

Aggression – Aggressive behavior or hostility is often observed in children and adolescents with ADHD, and has been reported in clinical trials and the postmarketing experience of some medications indicated for the treatment of ADHD. Although there is no systematic evidence that stimulants cause aggressive behavior or hostility, patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behavior or hostility.

Long-Term Suppression of Growth

Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development. Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of growth, however, it is anticipated that they likely have this effect as well. Therefore, growth should be monitored during treatment with stimulants, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

SEIZURES

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

VISUAL DISTURBANCE

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

USE IN CHILDREN UNDER SIX YEARS OF AGE

Methylin should not be used in children under 6 years, since safety and efficacy in this age group have not been established.

Drug Dependence

Methylin should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal from abusive use, since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that may require follow-up.

PRECAUTIONS

Patients with an element of agitation may react adversely; discontinue therapy if necessary.

Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

Drug treatment is not indicated in all cases of this behavioral syndrome and should be considered only in light of the complete history and evaluation of the child. The decision to prescribe Methylin should depend on the physician's assessment of the chronicity and severity of the child's symptoms and their appropriateness for his/her age. Prescription should not depend solely on the presence of one or more of the behavioral characteristics.

When these symptoms are associated with acute stress reactions, treatment with Methylin is usually not indicated.

Long-term effects of Methylin in children have not been well established.

DRUG INTERACTIONS

Methylin should not be used in patients being treated (currently or within the proceeding two weeks) with MAO Inhibitors (*see CONTRAINDICATIONS, Monoamine Oxidase Inhibitors*). Because of possible effects on blood pressure, Methylin should be used cautiously with pressor agents.

Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. Methylphenidate is metabolized primarily to ritalinic acid by de-esterification and not through oxidative pathways.

Methylin ER may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents.

Human pharmacologic studies have shown that racemic methylphenidate may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (e.g., phenobarbital, phenytoin, primidone), and tricyclic drugs (e.g., imipramine, clomipramine, desipramine).

Downward dose adjustments of these drugs may be required when given concomitantly with methylphenidate. It may be necessary to adjust the dosage and monitor plasma drug concentration (or, in case of coumarin, coagulation times), when initiating or discontinuing methylphenidate.

Serious adverse events have been reported in concomitant use with clonidine, although no causality for the combination has been established. The safety of using methylphenidate in combination with clonidine or other centrally acting alpha-2-agonists has not been systematically evaluated.

CARCINOGENESIS/MUTAGENESIS/IMPAIRMENT OF FERTILITY

In a lifetime carcinogenicity study carried out in B6C3F1 mice, methylphenidate caused an increase in hepatocellular adenomas and, in males only, an increase in hepatoblastomas, at a daily dose of approximately 60 mg/kg/day. This dose is approximately 30 times and 4 times the maximum recommended human dose on a mg/kg and mg/m² basis, respectively. Hepatoblastoma is a relatively rare rodent malignant tumor type. There was no increase in total malignant hepatic tumors. The mouse strain used is sensitive to the development of hepatic tumors, and the significance of these results to humans is unknown.

Methylphenidate did not cause any increases in tumors in a lifetime carcinogenicity study carried out in F344 rats; the highest dose used was approximately 45 mg/kg/day, which is approximately 22 times and 5 times the maximum recommended human dose on a mg/kg and mg/m² basis, respectively.

In a 24-week carcinogenicity study in the transgenic mouse strain p53+/-, which is sensitive to genotoxic carcinogens, there was no evidence of carcinogenicity. Male and female mice were fed diets containing the same concentration of methylphenidate as in the lifetime carcinogenicity study; the high-dose groups were exposed to 60 to 74 mg/kg/day of methylphenidate.

Methylphenidate was not mutagenic in the in vitro Ames reverse mutation assay or in the in vitro mouse lymphoma cell forward mutation assay. Sister chromatid exchanges and chromosome aberrations were increased, indicative of a weak clastogenic response, in an in vitro assay in cultured Chinese Hamster Ovary (CHO) cells. Methylphenidate was negative in vivo in males and females in the mouse bone marrow micronucleus assay.

Methylphenidate did not impair fertility in male or female mice that were fed diets containing the drug in an 18-week Continuous Breeding study. The study was conducted at doses up to 160 mg/kg/day, approximately 80-fold and 8-fold the highest recommended dose on a mg/kg and mg/m² basis, respectively.

PREGNANCY

Pregnancy Category C – In studies conducted in rats and rabbits, methylphenidate was administered orally at doses of up to 75 and 200 mg/kg/day, respectively, during the period of organogenesis. Teratogenic effects (increased incidence of fetal spina bifida) were observed in rabbits at the highest dose, which is approximately 40 times the maximum recommended human dose (MRHD) on a mg/m² basis. The no effect level for embryo-fetal development in rabbits was 60 mg/kg/day (11 times the MRHD on a mg/m² basis). There was no evidence of specific teratogenic activity in rats, although increased incidences of fetal skeletal variations were seen at the highest dose level (7 times the MRHD on a mg/m² basis), which was also maternally toxic. The no effect level for embryo-fetal development in rats was 25 mg/kg/day (2 times the MRHD on a mg/m² basis). When methylphenidate was administered to rats throughout pregnancy and lactation at doses of up to 45 mg/kg/day, offspring body weight gain was decreased at the highest dose (4 times the MRHD on a mg/m² basis), but no other effects on postnatal development were observed. The no effect level for pre- and postnatal development in rats was 15 mg/kg/day (equal to the MRHD on a mg/m² basis).

Adequate and well-controlled studies in pregnant women have not been conducted. Methylin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS

It is not known whether methylphenidate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised if Methylin is administered to a nursing woman.

PEDIATRIC USE

Long-term effects of methylphenidate in children have not been well established. Methylin should not be used in children under six years of age (*see* **WARNINGS**).

In a study conducted in young rats, methylphenidate was administered orally at doses of up to 100 mg/kg/day for 9 weeks, starting early in the postnatal period (Postnatal Day 7) and continuing through sexual maturity (Postnatal Week 10). When these animals were tested as adults (Postnatal Weeks 13 to 14), decreased spontaneous locomotor activity was observed in males and females previously treated with 50 mg/kg/day (approximately 6 times the maximum recommended human dose [MRHD] on a mg/m² basis) or greater, and a deficit in the acquisition of a specific learning task was seen in females exposed to the highest dose (12 times the MRHD on a mg/m² basis). The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (half the MRHD on a mg/m² basis). The clinical significance of the long-term behavioral effects observed in rats is unknown.

ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura); anorexia; nausea; dizziness; palpitations; headache; dyskinesia; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy. There have been rare reports of Tourette's syndrome. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking this drug: instances of abnormal liver function, ranging from transaminase elevation to hepatic coma; isolated cases of cerebral arteritis and/or occlusion; leukopenia and/or anemia; transient depressed mood; aggressive behavior; a few instances of scalp hair loss. Very rare reports of neuroleptic malignant syndrome (NMS) have been received, and, in most of these, patients were concurrently receiving therapies associated with NMS. In a single report, a ten-year-old boy who had been taking methylphenidate for approximately 18 months experienced an NMS-like event within 45 minutes of ingesting his first dose of venlafaxine. It is uncertain whether this case represented a drug-drug interaction, a response to either drug alone, or some other cause. In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

POSTMARKETING EXPERIENCE

In addition to the adverse events listed above, the following have been reported in patients receiving methylphenidate worldwide. The list is alphabetized: abnormal behavior, aggression, anxiety, cardiac arrest, depression, fixed drug eruption, hyperactivity, irritability, sudden death, suicidal behavior (including completed suicide), and thrombocytopenia. Data are insufficient to support an estimation of incidence or establish causation.

DOSAGE AND ADMINISTRATION

Dosage should be individualized according to the needs and responses of the patient.

ADULTS

Tablets: Administer in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. Patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

ER Tablets: Methylin ER tablets have a duration of action of approximately 8 hours. Therefore, Methylin ER tablets may be used in place of Methylin tablets when the 8-hour dosage of Methylin ER corresponds to the titrated 8-hour dosage of Methylin. Methylin ER tablets must be swallowed whole and never crushed or chewed.

CHILDREN (6 YEARS AND OVER)

Methylin should be initiated in small doses, with gradual weekly increments. Daily dosage above 60 mg is not recommended. If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

Tablets: Start with 5 mg twice daily (before breakfast and lunch) with gradual increments of 5 to 10 mg weekly.

ER Tablets: Methylin ER tablets have a duration of action of approximately 8 hours. Therefore, Methylin ER tablets may be used in place of Methylin tablets when the 8-hour dosage of Methylin ER corresponds to the titrated 8-hour dosage of Methylin. Methylin ER tablets must be swallowed whole and never crushed or chewed.

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.

Methylin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

OVERDOSAGE

Signs and symptoms of acute overdose, resulting principally from overstimulation of the central nervous system and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions

(may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis, and dryness of mucous membranes.


Consult with a Certified Poison Control Center regarding treatment for up-to-date guidance and advice.

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. Gastric contents may be evacuated by gastric lavage. In the presence of severe intoxication, use a carefully titrated dosage of a *short-acting* barbiturate before performing gastric lavage. Other measures to detoxify the gut include administration of activated charcoal and a cathartic.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

Efficacy of peritoneal dialysis or extracorporeal hemodialysis for Methylin overdosage has not been established.

HOW SUPPLIED

Each MethylinTM (methylphenidate HCl tablet USP) 5 mg is available as a round, white unscored tablet debossed with 5 on one side and a  on the other side.


Bottles of 100.....NDC 0406-1121-01

Bottles of 1000.....NDC 0406-1121-10

Each MethylinTM (methylphenidate HCl tablet USP) 10 mg is available as a round, white scored tablet debossed with 10 on one side of the tablet and a M on the other side.

Bottles of 100.....NDC 0406-1122-01

Bottles of 1000.....NDC 0406-1122-10


Each MethylinTM (methylphenidate HCl tablet USP) 20 mg is available as a round, white scored tablet debossed with 20 on one side of the tablet and a  on the other side.

Bottles of 100.....NDC 0406-1124-01


Bottles of 1000.....NDC 0406-1124-10

Protect from light. Dispense in tight, light-resistant container with child-resistant closure.

Storage: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Each MethylinTM ER (methylphenidate HCl extended-release tablet USP) 10 mg is available as a round, white to off-white tablet, debossed with 1423 on one side and a  on the other side.

Bottles of 100.....NDC 0406-1423-01

Each MethylinTM ER (methylphenidate HCl extended-release tablet USP) 20 mg is available as a round, white to off-white tablet, debossed with 1451 on one side and a  on the other side.


Bottles of 100.....NDC 0406-1451-01

Note: MethylinTM and MethylinTM ER tablets are color-additive free.

Dispense in tight, light-resistant container with child-resistant closure.

Storage: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Protect from moisture.

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Mallinckrodt Inc.,

Hazelwood, MO 63042 USA.

COVIDIENTM

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MEDICATION GUIDE

CII

MethylinTM (methylphenidate HCl tablets USP)

MethylinTM ER (methylphenidate HCl extended-release tablets USP)

Read the Medication Guide that comes with MethylinTM and MethylinTM ER before you or your child starts taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about your or your child's treatment with MethylinTM and MethylinTM ER.

What is the most important information I should know about MethylinTM and MethylinTM ER?

The following have been reported with use of MethylinTM and MethylinTM ER and other stimulant medicines.

1. Heart-related problems:

- **sudden death in patients who have heart problems or heart defects**
- **stroke and heart attack in adults**
- **increased blood pressure and heart rate**

Tell your doctor if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.

Your doctor should check you or your child carefully for heart problems before starting MethylinTM and MethylinTM ER.

Your doctor should check your or your child's blood pressure and heart rate regularly during treatment with MethylinTM and MethylinTM ER.

Call your doctor right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking MethylinTM and MethylinTM ER.

2. Mental (Psychiatric) problems:

All Patients

- **new or worse behavior and thought problems**
- **new or worse bipolar illness**
- **new or worse aggressive behavior or hostility**

Children and Teenagers

- **new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms**

Tell your doctor about any mental problems you or your child have, or about a family history of suicide, bipolar illness, or depression.

Call your doctor right away if you or your child have any new or worsening mental symptoms or problems while taking MethylinTM and MethylinTM ER, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What Is MethylinTM and MethylinTM ER?

MethylinTM and MethylinTM ER is a central nervous system stimulant prescription medicine. **It is used for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD).** MethylinTM and MethylinTM ER may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

MethylinTM and MethylinTM ER should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

MethylinTM and MethylinTM ER is also used in the treatment of a sleep disorder called narcolepsy.

MethylinTM and MethylinTM ER is a federally controlled substance (CII) because it can be abused or lead to dependence. Keep MethylinTM and MethylinTM ER in a safe place to prevent misuse and abuse. Selling or giving away MethylinTM and MethylinTM ER may harm others, and is against the law.

Tell your doctor if you or your child have (or have a family history of) ever abused or been dependent on alcohol, prescription medicines or street drugs.

Who should not take MethylinTM and MethylinTM ER?

MethylinTM and MethylinTM ER should not be taken if you or your child:

- are very anxious, tense, or agitated
- have an eye problem called glaucoma
- have tics or Tourette's syndrome, or a family history of Tourette's syndrome. Tics are hard to control repeated movements or sounds.
- are taking or have taken within the past 14 days an antidepressant medicine called a monoamine oxidase inhibitor or MAOI.
- are allergic to anything in MethylinTM and MethylinTM ER. See the end of this Medication Guide for a complete list of ingredients.

MethylinTM and MethylinTM ER should not be used in children less than 6 years old because it has not been studied in this age group.

MethylinTM and MethylinTM ER may not be right for you or your child. Before starting MethylinTM and MethylinTM ER tell your or your child's doctor about all health conditions (or a family history of) including:

- heart problems, heart defects, high blood pressure
- mental problems including psychosis, mania, bipolar illness, or depression
- tics or Tourette's syndrome
- liver or kidney problems
- seizures or have had an abnormal brain wave test (EEG)

Tell your doctor if you or your child is pregnant, planning to become pregnant, or breastfeeding.

Can MethylinTM and MethylinTM ER be taken with other medicines?

Tell your doctor about all of the medicines that you or your child take including prescription and nonprescription medicines, vitamins, and herbal supplements. MethylinTM and MethylinTM ER and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking MethylinTM and MethylinTM ER. Your doctor will decide whether MethylinTM and MethylinTM ER can be taken with other medicines.

Especially tell your doctor if you or your child takes:

- antidepressant medicines including MAOIs
- seizure medicines
- blood thinner medicines
- blood pressure medicines
- cold or allergy medicines that contain decongestants

Know the medicines that you or your child takes. Keep a list of your medicines with you to show your doctor and pharmacist.

Do not start any new medicine while taking MethylinTM and MethylinTM ER without talking to your doctor first.

How should MethylinTM and MethylinTM ER be taken?

- **Take MethylinTM and MethylinTM ER exactly as prescribed.** Your doctor may adjust the dose until it is right for you or your child.
- MethylinTM is usually taken 2 to 3 times a day.
- Take MethylinTM and MethylinTM ER 30 to 45 minutes before a meal.
- The effect of a dose of MethylinTM ER usually lasts about 8 hours.
- **Do not chew or crush MethylinTM ER tablets.** Swallow MethylinTM ER tablets whole with water or other liquids. Tell your doctor if you or your child cannot swallow MethylinTM ER whole. A different medicine may need to be prescribed.
- From time to time, your doctor may stop MethylinTM and MethylinTM ER treatment for awhile to check ADHD symptoms.

- Your doctor may do regular checks of the blood, heart, and blood pressure while taking MethylinTM and MethylinTM ER. Children should have their height and weight checked often while taking MethylinTM and MethylinTM ER. MethylinTM and MethylinTM ER treatment may be stopped if a problem is found during these check-ups.
- **If you or your child takes too much MethylinTM and MethylinTM ER or overdoses, call your doctor or poison control center right away, or get emergency treatment.**

What are possible side effects of MethylinTM and MethylinTM ER?

See “What is the most important information I should know about MethylinTM and MethylinTM ER?” for information on reported heart and mental problems.

Other serious side effects include:

- slowing of growth (height and weight) in children
- seizures, mainly in patients with a history of seizures
- eyesight changes or blurred vision

Common side effects include:

-
- | | |
|--------------------|----------------------|
| • headache | • decreased appetite |
| • stomach ache | • nervousness |
| • trouble sleeping | • dizziness |
| • nausea | • heart palpitations |
-

Talk to your doctor if you or your child has side effects that are bothersome or do not go away.

This is not a complete list of possible side effects. Ask your doctor or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store MethylinTM and MethylinTM ER?

- Store MethylinTM and MethylinTM ER in a safe place at room temperature, 68° to 77°F (20° to 25°C).
- Protect MethylinTM from light.
- Protect MethylinTM ER from moisture.
- **Keep MethylinTM and MethylinTM ER and all medicines out of the reach of children.**

General information about MethylinTM and MethylinTM ER

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use MethylinTM and MethylinTM ER for a condition for which it was not prescribed. Do not give MethylinTM and MethylinTM ER to other people, even if they have the same condition. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about MethylinTM and MethylinTM ER. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about MethylinTM and MethylinTM ER that was written for healthcare professionals, or you can visit www.Mallinckrodt.com or call 1-800-778-7898.

What are the ingredients in MethylinTM and MethylinTM ER?

Active Ingredient: methylphenidate HCl

Inactive Ingredients:

MethylinTM tablets: lactose monohydrate, magnesium stearate, microcrystalline cellulose, and talc.

MethylinTM ER tablets: hydroxypropyl methylcellulose 2208, magnesium stearate, microcrystalline cellulose, and talc.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Mallinckrodt Inc.,

Hazelwood, MO 63042 USA.

COVIDIEN™

Mallinckrodt

Rev 011409

PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - 5 MG BOTTLE

NDC 0406-1121-10

1000 TABLETS

Methylin™

CII

methylphenidate HCl tablets USP

5 mg

Rx only

Each tablet contains:

Methylphenidate Hydrochloride USP 5 mg

This package is not for household use.

PHARMACIST: PLEASE DISPENSE WITH
MEDICATION GUIDE PROVIDED WITH PRODUCT

Mallinckrodt

USUAL DOSAGE:

See package insert.

STORAGE:

Store at 20° to 25°C

(68° to 77°F) [see USP Controlled

Room Temperature].

Protect from light.

Dispense in tight, light-resistant
container with child-resistant
closure.

Do not accept if seal over bottle
opening is broken or missing.

Mallinckrodt Inc.,

Hazelwood, MO 63042 USA.

COVIDIEN™

L00M13

Rev 011409



PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - 10 MG BOTTLE

NDC 0406-1122-10

1000 TABLETS

Methylin™

CII

methylphenidate HCl tablets USP

10 mg

Rx only

Each tablet contains:

Methylphenidate Hydrochloride USP 10 mg

This package is not for household use.

PHARMACIST: PLEASE DISPENSE WITH
MEDICATION GUIDE PROVIDED WITH PRODUCT

Mallinckrodt

USUAL DOSAGE:

See package insert.

STORAGE:

Store at 20° to 25°C
(68° to 77°F) [see USP Controlled
Room Temperature].

Protect from light.

Dispense in tight, light-resistant
container with child-resistant
closure.

Do not accept if seal over bottle
opening is broken or missing.

Mallinckrodt Inc.,
Hazelwood, MO 63042 USA.

COVIDIEN™

L00M15

Rev 011409

**PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - 20 MG BOTTLE**

NDC 0406-1124-10

1000 TABLETS

Methylin™

CII

methylphenidate HCl tablets USP

20 mg

Rx only

Each tablet contains:

Methylphenidate Hydrochloride USP 20 mg

This package is not for household use.

PHARMACIST: PLEASE DISPENSE WITH
MEDICATION GUIDE PROVIDED WITH PRODUCT

Mallinckrodt

USUAL DOSAGE:

See package insert.

STORAGE:

Store at 20° to 25°C
(68° to 77°F) [see USP Controlled
Room Temperature].

Protect from light.

Dispense in tight, light-resistant
container with child-resistant
closure.

Do not accept if seal over bottle
opening is broken or missing.

Mallinckrodt Inc.,
Hazelwood, MO 63042 USA.

COVIDIEN™

L00M17

Rev 011409

Exp.: Lot No.:
N 0406-1124-102
L00M17 Rev 011409
NO VARNISH

NDC 0406-1124-10 1000 TABLETS

Methylin™ CII
methylphenidate HCl tablets USP

20 mg Rx only

Each tablet contains:
Methylphenidate Hydrochloride USP 20 mg
This package is not for household use.

PHARMACIST: PLEASE DISPENSE WITH
MEDICATION GUIDE PROVIDED WITH PRODUCT

Mallinckrodt

USUAL DOSAGE:
See package insert.

STORAGE: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Protect from light.

Dispense in tight, light-resistant container with child-resistant closure.

Do not accept if seal over bottle opening is broken or missing.

Mallinckrodt Inc.,
Hazelwood, MO 63042 USA.

COVIDIEN™

PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - 10 MG BOTTLE

NDC 0406-1423-01

100 TABLETS

Methylin™ ER

CII

methylphenidate HCl extended-release tablets USP

10 mg

Rx only

Each tablet contains: Methylphenidate Hydrochloride USP 10 mg

PHARMACIST: PLEASE DISPENSE WITH

MEDICATION GUIDE PROVIDED WITH PRODUCT

Mallinckrodt

USUAL DOSAGE: See package insert.

STORAGE: Store at 20° to 25°C (68° to 77°F)

[see USP Controlled Room Temperature].

Protect from moisture.

Dispense in tight, light-resistant container with child-resistant closure.

Do not accept if seal over bottle opening is broken or missing.

Mallinckrodt Inc.,

Hazelwood, MO 63042 USA.

COVIDIEN™

L00M18

Rev 011409

Exp.: Lot No.:
N 0406-1423-014
L00M18 Rev 011409
NO VARNISH

NDC 0406-1423-01 100 TABLETS

Methylin™ ER
methylphenidate HCl extended-release tablets USP

10 mg Rx only

Each tablet contains: Methylphenidate Hydrochloride USP 10 mg

PHARMACIST: PLEASE DISPENSE WITH
MEDICATION GUIDE PROVIDED WITH PRODUCT

Mallinckrodt

USUAL DOSAGE: See package insert.

STORAGE: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Protect from moisture.

Dispense in tight, light-resistant container with child-resistant closure.

Do not accept if seal over bottle opening is broken or missing.

Mallinckrodt Inc.,
Hazelwood, MO 63042 USA.

COVIDIEN™

PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - 20 MG BOTTLE

NDC 0406-1451-01

100 TABLETS

Methylin™ ER

CII

methylphenidate HCl extended-release tablets USP

20 mg

Rx only

Each tablet contains: Methylphenidate Hydrochloride USP 20 mg

PHARMACIST: PLEASE DISPENSE WITH
MEDICATION GUIDE PROVIDED WITH PRODUCT

Mallinckrodt

USUAL DOSAGE: See package insert.

STORAGE: Store at 20° to 25°C (68° to 77°F)

[see USP Controlled Room Temperature].

Protect from moisture.

Dispense in tight, light-resistant container
with child-resistant closure.

Do not accept if seal over bottle opening
is broken or missing.

Mallinckrodt Inc.,

Hazelwood, MO 63042 USA.

COVIDIEN™

L00M19

Rev 011409



Revised: 06/2009

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